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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,916	07/09/2001	Hiroshi Shiku	P20854	1184
7055	7590	12/20/2004	EXAMINER	
GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191			EWOLDT, GERALD R	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/787,916

Applicant(s)

SHIKU ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2004 and 02 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/2/4</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The finality of the Office Action, mailed 4/21/04 has been withdrawn.
2. Claims 1-20 are being acted upon.
3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. Claims 13 and 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Jiang et al. (1995, of record).

As set forth previously,

Nestle et al. teaches a method for inducing cellular immunity comprising isolating a dendritic cell (DC) antigen presenting cell (APC), reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration (see particularly Methods, page 331, column 2 - page 332, column 1).

The reference teaching differs from the claimed invention only in that it does not teach the reaction of the APC with a complex comprising a hydrophobized polysaccharide.

Jiang et al. teaches that the dendritic cell (DC) homolog of the macrophage mannose receptor (DEC-205) can facilitate a 100-fold increase in the uptake and presentation of antigen by a DC (see particularly page 154, Figure 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for inducing cellular immunity comprising isolating an APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al., including a hydrophobized polysaccharide complex (such as mannan) in the reacting of the antigen with the APC. One of ordinary skill in the art at the time of the invention would have been motivated to add a mannan complex to the reaction because said addition would have been

expected to increase the uptake and presentation by the DC, given the teachings of Jiang et al. that activation of the DC homolog of the macrophage mannose receptor (DEC-205) can facilitate a 100-fold increase in the uptake and presentation of antigen by a DC.

Applicant's arguments, filed 10/15/04, have been fully considered but they are not persuasive. Applicant again argues that one of ordinary skill would not have been motivated to combine the references and that the combined references do not teach reacting a complex comprising a hydrophobized polysaccharide and an antigen with the antigen-presenting cell. Applicant also appears to be unclear as to how the references have been combined. Applicant further argues that the polysaccharide of the prior art cannot form a complex with a tumor antigen.

Regarding the combination of references, the primary reference teaches a method comprising the *in vitro* loading of APCs with a tumor antigen and the return of said cells to a living body for the induction of a cellular immune response. The secondary reference teaches that the binding of the mannan receptor DEC-205 can facilitate the uptake and presentation of antigen by an APC. Thus, these teachings along with sound scientific reasoning would render the claimed method, i.e., employing a hydrophobized polysaccharide-antigen complex (which would bind the DEC-205 receptor) for the facilitated loading of APCs and the subsequent return of the APCs into a living body for the induction of a cellular immune response, an obvious improvement over the combined method of the prior art to the ordinarily skilled artisan.

Regarding the "complex" of the instant claims versus the combined polysaccharide and antigen of the prior art, given the broad definitions in the specification, the "complex" of the claims would encompass the polysaccharide and antigen of the prior art. The antigens at page 5 are disclosed as being any "substances that induce immunity". The polysaccharides of the instant claims are defined at page 6 as, "Polysaccharides constituting the hydrophobized polysaccharide are polymers composed of monosaccharide residues linked each other by glycoside bonds". While several examples of complexes encompassed by the method of the instant claims are disclosed, in each case it is further disclosed that the examples are not intended to be limiting. Examples of methods of preparing the complexes are disclosed at pages 6-7 employing language such as "may include" or "may have", which is clearly not limiting.

Accordingly, it remains the Examiner's position that the combined references comprise an improved method and render the method of the instant claims obvious.

5. The following are new grounds for rejection necessitated by Applicant's amendment and IDS, filed 7/02/04.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

7. Claims 1-3, 6, 11, 12, 15, 18 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kohno et al. 1996.

Kohno et al. teaches a DC APC capable of inducing cellular immunity, said cell having been produced by reacting *in vitro* with the hydrophobized polysaccharide pullulan (see particularly page 213, column 1).

The reference clearly anticipates the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1997, IDS).

Nestle et al. has been discussed above and previously.

The reference differs from the claimed invention only in that it does not teach an APC loaded with the ErbB-2 antigen by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen (an antigen overexpressed in a wide range of human adenocarcinomas, see Abstract) can be used to induce CD8+ CTLs (page 19, column 2, second full paragraph and page 23, column 1) by a mechanism of facilitating the entry of the antigen into the MHC Class I pathway for presentation by APCs (see particularly page 24, column 1, first full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen of Gu et al. given the teachings of the reference that the ErbB-2 antigen is overexpressed in a wide range of human adenocarcinomas (and would thus provide an obvious target for immunotherapy) and that the use of the cholesterol bearing mannan polysaccharide facilitates the entry of the antigen into the MHC Class I pathway for presentation by APCs.

10. No claim is allowed.

11. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner

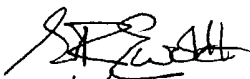
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can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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12/14/87
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